SEQUENCE LISTING

<110> Hiroshi MORI

<120> Gamma-secretase Inhibitor

<130> GP59-PCT

<150> JP 2002-121983

<151> 2002-04-14

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<212> PRT

<213> Homo sapiens

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Lys

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														att		192
Asn		Lys	Trp	Asp	Ser		Pro	Ser	Gly	ihr		Ihr	Uys	He	Asp	
	50					55					60					
acc	aag	gaa	ggc	atc	ctg	cag	tat	tgc	caa	gaa	gtc	tac	cct	gaa	ctg	240
Thr	Lys	Glu	Gly	He	Leu	Gln	Tyr	Cys	Gln	Glu	Val	Tyr	Pro	Glu	Leu	
65					70					75	٠				80	
cag	atc	acc	aat	gtg	gta	gaa	gcc	aac	caa	cca	gtg	acc	atc	cag	aac	288
														Gln		
			,	85					90					95		
†øø	tøc	аад	Cee	ggc	cgc	aag	cag	tgc	aag	acc	cat	CCC	cac	ttt	gtg	336
														Phe		
,		_,	100		Ū			105					110			
2++	000	tac	cac	tac	tta	σtt	σσt	σaσ	+++	gta	agt	gat	gCC	ctt	ctc	384
															Leu	
	.,,	115		•,•			120					125				
-++	oo+	~~~	200	+ ~~	000	++0	++0	000	000	g a g	200	atσ	σat	σtt	tøc	432
															tgc Cys	102
Vai	130		Lyo	0,0	Lyo	135			4111	4.4	140					
	100					100										
								4					+ ~ ~	oat	gog	480
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		піъ	Leu	птъ			1111	Vai	на			1111	Oyo	001	Glu 160	
145					150					155					100	
aag	agt	acc	aac	ttg	cat	gac	tac	ggc	atg	ttg	ctg	ccc	tgc	gga	att	528

_ys	Ser	Thr	Asn	Leu 165	His	Asp	Tyr	Gly	Met 170	Leu	Leu	Pro	Cys	Gly 175	lle	
					gta Val											576
					tct Ser											624
					gac Asp							Ser				672
					gag Glu 230	Glu					Glu					720
					Glu					Gly					gaa Glu	768
				Pro	tac Tyr				Thr					Ser		816
			Thr					Glu					Val		cga Arg	864

-								•			gtt Val 300					912
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											tcc Ser					1008
											ttg Leu					1056
			Val					Gln			gtg Val		Ser			1104
											gag Glu 380	Thr				1152
_						Asn					ctg Leu					1200
tac	atc	acc	gct	ctg	cag	gct	gtt	cct	cct	cgg	cct	cgt	cac	gtg	ttc	1248

Tyr	lle	Thr	Ala		Gln	Ala	Val	Pro	Pro	Arg	Pro	Arg	His		Phe	
				405					410					415		
oo+	ot a	oto	οοσ	aan	+a+	αtο	cac	aca	gaa	cag	аар	gac	aga	CAF	cac	1296
									Glu							
,,,,,,			420	_,				425					430			
acc	cta	aag	cat	ttc	gag	cat	gtg	cgc	atg	gtg	gat	ccc	aag	aaa	gcc	1344
Thr	Leu	Lys	His	Phe	Glu	His	Val	Arg	Met	Val	Asp	Pro	Lys	Lys	Ala	
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gct	cag	atc	cgg	tcc	cag	gtt	atg	aca	cac	ctc	cgt	gtg	att	tat	gag	1392
Ala	Gln	He	Arg	Ser	Gln	Val	Met	Thr	His	Leu	Arg	Val	He	Tyr	Glu	
	450					455					460					
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Arg	Met	Asn	Gln	Ser	Leu	Ser	Leu	Leu	Tyr	Asn	Val	Pro	Ala	Val	Ala	
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Glu	Glu	He	Gln			Val	Asp	Glu			GIn	Lys	Glu		Asn	
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															agt	1536
Tyr	Ser	Asp			Leu	Ala	Asr			Ser	Giu	Pro			Ser	
			500	1				505	•				510	1		
																4504
															acc	1584
Tyr	Gly			Ala	Leu	Met			Leu	ınr	GIU			ınr	Thr	
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				ctt Leu													1632
F				tct Ser													1680
				cct Pro													1728
				ggt Gly 580													1776
				atg Met					Arg					Tyr			1824
			Gln	aaa Lys				Phe					Gly				1872
		Ala		att Ile			Met					Val					1920
	atc	gtc	atc	acc	ttg	gtg	atg	ctg	aag	aag	aaa	cag	; tac	aca	tcc	att	1968

He	Val	He	Thr	Leu 645	Val	Met	Leu	Lys	Lys 650	Lys	GIn	Tyr	Thr	Ser 655	lle		
a.a.t	+		-4-	_4_		_11			4	_1_						0.	016
				•									gag Glu			20	016
			660					665					670				
cac	ctg	tcc	aag	atg	cag	cag	aac	ggC	tac	gaa	aat	cca	acc	tac	aag	20	064
					_	_				_			Thr		_	_	
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Phe Phe Glu Gln Met Gln Asn
690 695

<210> 7

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<400> 7

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- GIn Ile Ala Met Phe Cys Gly Arg Leu Asn Met His Met Asn Val Gln 35 40 45
- Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp
 50 55 60
- Thr Lys Glu Gly 11e Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu 65 70 75 80
- Gln lle Thr Asn Val Val Glu Ala Asn Gln Pro Val Thr lle Gln Asn 85 90 95
- Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val
- Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu 115 120 125
- Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys 130 135 140
- Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu 145 150 155 160
- Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly IIe 165 170 175
- Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu
 180 185 190
- Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val

		195					200					205			
Trp	Trp 210	Gly	Gly	Ala	Asp	Thr 215	Asp	Tyr	Ala	Asp	Gly 220	Ser	Glu	Asp [·]	Lys
Va I 225	Val	Glu	Val	Ala	Glu 230	Glu	Glu	Glu	Val	Ala 235	Glu	Val	Glu	Glu	G1u 240
Glu	Ala	Asp	Asp	Asp 245	Glu	Asp	Asp	Glu	Asp 250	Gly	Asp	Glu	Val	GIu 255	Glu
Glu	Ala	Glu	GIu 260	Pro	Tyr	Glu	Glu	Ala 265	Thr	Glu	Arg	Thr	Thr 270	Ser	He
Ala	Thr	Thr 275	Thr	Thr	Thr	Thr	Thr 280	Glu	Ser	Val	Glu	Glu 285	Val	Val	Arg
Val	Pro 290	Thr	Thr	Ala	Ala	Ser 295	Thr	Pro	Asp	Ala	Va I 300	Asp	Lys	Tyr	Leu
G I u 305	Thr	Pro	Gly	Asp	Glu 310	Asn	Glu	His	Ala	His 315	Phe	Gin	Lys	Ala	Lys 320
Glu	Arg	Leu	Glu	Ala 325	Lys	His	Arg	Glu	Arg 330	Met	Ser	Gln	Val	Met 335	Arg
Glu	Trp	Glu	Glu 340	Ala	Glu	Arg	GIn	Ala 345	Lys	Asn	Leu	Pro	Lys 350	Ala	Asp

Lys Lys Ala Val Ile Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu

365

360

355

- Gln Glu Ala Asn Glu Arg Gln Gln Leu Val Glu Thr His Met Ala 370 375 380
- Arg Val Glu Ala Met Leu Asn Asp Arg Arg Arg Leu Ala Leu Glu Asn 385 390 395 400
- Tyr IIe Thr Ala Leu Gln Ala Val Pro Pro Arg Pro Arg His Val Phe 405 410 415
- Asn Met Leu Lys Lys Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His
 420 425 430
- Thr Leu Lys His Phe Glu His Val Arg Met Val Asp Pro Lys Lys Ala 435 440 445
- Ala Gln lle Arg Ser Gln Val Met Thr His Leu Arg Val lle Tyr Glu 450 455 460
- Arg Met Asn Gln Ser Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala 465 470 475 480
- Glu Glu Ile Gln Asp Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn 485 490 495
- Tyr Ser Asp Asp Val Leu Ala Asn Met IIe Ser Glu Pro Arg IIe Ser 500 505 510
- Tyr Gly Asn Asp Ala Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr
 515 520 525

- Val Glu Leu Leu Pro Val Asn Gly Glu Phe Ser Leu Asp Asp Leu Gln 530 535 540
- Pro Trp His Ser Phe Gly Ala Asp Ser Val Pro Ala Asn Thr Glu Asn 545 550 555 560
- Glu Val Glu Pro Val Asp Ala Arg Pro Ala Ala Asp Arg Gly Leu Thr
 565 570 575
- Thr Arg Pro Gly Ser Gly Leu Thr Asn IIe Lys Thr Glu Glu IIe Ser 580 590
- Glu Val Lys Met Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val 595 600 605
- His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys 610 615 620
- Gly Ala IIe IIe Gly Leu Met Val Gly Gly Val Val IIe Ala Thr Val 625 630 635 640
- Ile Val Ile Thr Leu Val Met Leu Lys Lys Gln Tyr Thr Ser Ile 645 650 655
- His His Gly Val Val Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg 660 665 670
- His Leu Ser Lys Met Gln Gln Asn Gly Tyr Glu Asn Pro Thr Tyr Lys 675 680 685

Phe Phe Glu Gln Met Gln Asn

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<212> DNA

<213> Homo sapiens

<400> 8

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gcg ctg gag gta ccc act gat ggt aat gct ggc ctg ctg gct gaa ccc 96
Ala Leu Glu Val Pro Thr Asp Gly Asn Ala Gly Leu Leu Ala Glu Pro
20 25 30

cag att gcc atg ttc tgt ggc aga ctg aac atg cac atg aat gtc cag

144

Gin ile Ala Met Phe Cys Gly Arg Leu Asn Met His Met Asn Val Gin

35

40

45

aat ggg aag tgg gat tca gat cca tca ggg acc aaa acc tgc att gat

192
Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp
50
55
60

acc aag gaa ggc atc ctg cag tat tgc caa gaa gtc tac cct gaa ctg

Thr Lys Glu Gly Ile Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu

70 75 80

cag	atc	acc	aat	gtg	gta	gaa	gcc	aac	caa	cca	gtg	acc	atc	cag	aac	288	
Gln	lle	Thr	Asn	Va I 85	Val	Glu	Ala	Asn	GIn 90	Pro	Val	Thr	He	GIn 95	Asn		
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Trp	Cys	Lys	Arg 100	Gly	Arg	Lys	GIn	Cys 105	Lys	Thr	His	Pro	His 110	Phe	Val		
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lle	Pro	Tyr 115	Arg	Cys	Leu	Val	Gly 120		Phe	Val	Ser	Asp 125	Ala	Leu	Leu		
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Val	Pro 130	Asp	Lys	Cys	Lys	Phe 135	Leu	His	Gln	Glu	Arg 140	Met	Asp	Val	Cys		
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Glu 145	Thr	His	Leu	His	Trp 150	His	Thr	Val	Ala	Lys 155	Glu	Thr	Cys	Ser	Glu 160		
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Lys	Ser	Thr	Asn	Leu 165	His	Asp	Tyr	Gly	Met 170	Leu	Leu	Pro	Cys	Gly 175	He		
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Asp	Lys ·	Phe	Arg 180	Gly	Val	Glu	Phe	Va I 185	Cys	Cys	Pro	Leu	Ala 190	Glu	Glu		

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Ser	Asp	Asn 195	Val	Asp	Ser	Ala	Asp 200	Ala	Glu	Glu	Asp	Asp 205	Ser	Asp	Val	
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Trp	Trp 210	Gly	Gly	Ala	Asp	Thr 215	Asp	Tyr	Ala	Asp	Gly 220	Ser	Glu	Asp	Lys	
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Va I 225	Val	Glu	Val	Ala	Glu 230	Glu	Glu	Glu	Val	Ala 235	Glu	Val	Glu	Glu	Glu 240	
gaa	gcc	gat	gat	gac	gag	gac	gat	gag	gat	ggt	gat	gag	gta	gag	gaa	768
Glu	Ala	Asp	Asp	Asp 245	Glu	Asp	Asp	Glu	Asp 250	Gly	Asp	Glu	Val	Glu 255	Glu	
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Glu	Ala	Glu	GIu 260	Pro	Tyr	Glu	Glu	Ala 265	Thr	Glu	Arg	Thr	Thr 270	Ser	lle	
gcc	acc	acc	acc	асс	acc	acc	aca	gag	tct	gtg	gaa	gag	gtg	gtt	cga	864
Ala	Thr	Thr 275	Thr	Thr	Thr	Thr	Thr 280	Glu	Ser	Val	Glu	Glu 285	Val	Val	Arg	
gag	gtg	tgc	tct	gaa	caa	gcc	gag	acg	ggg	ccg	tgc	cga	gca	atg	atc	912
Glu	Va I 290	Cys	Ser	Glu	GIn	Ala 295	Glu	Thr	Gly	Pro	Cys 300	Arg	Ala	Met	lle	

960

tcc cgc tgg tac ttt gat gtg act gaa ggg aag tgt gcc cca ttc ttt

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Ser . 305	Arg	Trp	Tyr	Phe	Asp 310	Val	Thr	Glu	Gly	Lys 315	Cys	Ala	Pro	Phe	Phe 320		
tac	g g C	gga	tøt	PPC	-ggC	aac	CEE	aac	aac	ttt	gac	aca	gaa	gag	tac	1008	,
		Gly															
•				325					330					335			
	.		_4_	.			~~~	a+ -	+		0.4	++0	oto	225	act	1056	
		gcc														1030	,
Cys	Met	Ala	340	Cys	GIY	Ser	Ala	мет 345	Ser	GIN	3er	Leu	350	Lys	1111		
										•							
acc	cag	gaa	cct	ctt	ggc	cga	gat	cct	gtt	aaa	ctt	cct	aca	aca	gca	1104	1
Thr	Gln		Pro	Leu	Gly	Arg		Pro	Val	Lys	Leu			Thr	Ala		
		355					360					365	•				
gcc	agt	acc	cct	gat	gcc	g††	gac	aag	tat	ctc	gag	aca	cct	ggg	gat	1152	2
															Asp		
ΛIα	370		110	nop	711 W	375		_,0	.,.		380		• • •	3			
gag	aat	gaa	cat	gcc	cat	ttc	cag	aaa	gcc	aaa	gag	agg	ctt	gag	gcc	120	0
Glu	Asn	Glu	His	Ala			Gln	Lys	Ala			Arg	Leu	Glu	Ala		
385					390					395					400		
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															gca	124	0
Lys	His	Arg	Glu	Arg 405		Ser	GIn	Val	Met 410		; Glu	ırp	Glu	1 GIL 415	ı Ala		
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gaa	cgt	caa	gca	aag	aac	ttg	cct	aaa	gct	gat	aag	aag	gca	gtt	atc	1296
Glu	Arg	Gln	Ala 420	Lys	Asn	Leu	Pro	Lys 425	Ala	Asp	Lys	Lys	Ala 430	Val	lle	
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GIn	His	Phe 435	GIn	Glu	Lys	Val	GIu 440	Ser	Leu	Glu	GIn	Glu 445	Ala	Ala	Asn	
gag	aga	cag	cag	ctg	gtg	gag	aca	cac	atg	gcc	aga	gtg	gaa	gcc	atg	1392
Gļu	Arg 450	Gln	Gln	Leu	Val	G1u 455	Thr	His	Met	Ala	Arg 460	Val	Glu	Ala	Met	
ctc	aat	gac	cgc	cgc	cgc	ctg	gcc	ctg	gag	aac	tac	atc	асс	gct	ctg	1440
Leu 465	Asn	Asp	Arg	Arg	Arg 470	Leu	Ala	Leu	Glu	Asn 475	Tyr	lle	Thr	Ala	Leu 480	
cag	gct	gtt	cct	cct	cgg	cct	cgt	cac	gtg	ttc	aat	atg	cta	aag	aag	1488
Gln	Ala	Val	Pro	Pro 485	Arg	Pro	Arg	His	Val 490	Phe	Asn	Met	Leu	Lys 495	Lys	
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Tyr	Val	Arg	Ala 500	Glu	GIn	Lys	Asp	Arg 505	Gln	His	Thr	Leu	Lys 510	His	Phe	
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Glu	His	Va I 515	Arg	Met	Val	Asp	Pro 520	Lys	Lys	Ala	Ala	GIn 525	lle	Arg	Ser	

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Gln	Va I 530	Met	Thr	His	Leu	Arg 535	Val	lle	Tyr	Glu	Arg 540	Met	Asn	Gln	Ser	
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Leu 545	Ser	Leu	Leu	Tyr	A sn 550	Val	Pro	Ala	Val	Ala 555	Glu	Glu	lle	GIn	Asp 560	
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									atc							1776
Leu	АТА	ASI	мет 580	ile	ser	GIU	Pro	585	lle	ser	ıyr	ч	590	ASP	на	
ctc	atg	cca	tct	ttg	acc	gaa	acg	aaa	acc	acc	gtg	gag	ctc	ctt	CCC	1824
Leu	Met	Pro 595	Ser	Leu	Thr	Glu	Thr 600	Lys	Thr	Thr	Val	Glu 605	Leu	Leu	Pro	
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Val	Asn 610	Gly	Glu	Phe	Ser	Leu 615	Asp	Asp	Leu	GIn	Pro 620	Trp	His	Ser	Phe	
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ggg	gct	gac	tct	gtg	cca	gcc	aac	aca	gaa	aac	gaa	gtt	gag	cct	gtt	1920
Gly 625	Ala	Asp	Ser	Val	Pro 630	Ala	Asn	Thr	Glu	Asn 635	Glu	Val	Glu		Val 640	

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Asp Ala Arg	Pro Ala Ala 645	Asp Arg Gly	Leu Thr Thr 650	Arg Pro Gly 655	Ser
ggg ttg aca	aat atc aag	acg gag gag	atc tct gaa	gtg aag atg	gat 2016
Gly Leu Thr			lle Ser Glu		Asp
	660	665		670	•
		tca gga tat			
Ala Glu Phe	Arg HIS ASP	Ser Gly Tyr 680	Giu vai nis	685	Leu
gtg ttc ttt	gca gaa gat	gtg ggt tca	aac aaa ggt	gca atc att	gga 2112
		Val Gly Ser			
690		695	700		
ctc atg gtg	ggc ggt gtt	gtc ata gcg	aca gtg atc	gtc atc acc	ttg 2160
		Val lle Ala	·	Val IIe Thr	
705	710		715		720
		cag tac aca			•
Val Met Leu	Lys Lys Lys 725	Gln Tyr Thr	730	735	
gag gtt gac	gcc gct gtc	acc cca gag	gag cgc cac	ctg tcc aag	atg 2256
		Thr Pro Glu			
·	740	745		750	

cag cag aac ggc tac gaa aat cca acc tac aag ttc ttt gag cag atg

Gin Gin Asn Giy Tyr Giu Asn Pro Thr Tyr Lys Phe Phe Giu Gin Met

755

760

765

cag aac tag

2313

GIn Asn 770

<210> 9

<211> 770

<212> PRT

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Ala Leu Glu Val Pro Thr Asp Gly Asn Ala Gly Leu Leu Ala Glu Pro 20 25 30

Gin Ile Ala Met Phe Cys Gly Arg Leu Asn Met His Met Asn Val Gin 35 40 45

Asn Gly Lys Trp Asp Ser Asp Pro Ser Gly Thr Lys Thr Cys Ile Asp 50 55 60

Thr Lys Glu Gly He Leu Gln Tyr Cys Gln Glu Val Tyr Pro Glu Leu 65 70 75 80

Gin He Thr Asn Val Val Glu Ala Asn Gin Pro Val Thr He Gin Asn 85 90 95

Trp Cys Lys Arg Gly Arg Lys Gln Cys Lys Thr His Pro His Phe Val

Ile Pro Tyr Arg Cys Leu Val Gly Glu Phe Val Ser Asp Ala Leu Leu 115 120 125

Val Pro Asp Lys Cys Lys Phe Leu His Gln Glu Arg Met Asp Val Cys 130 135 140

Glu Thr His Leu His Trp His Thr Val Ala Lys Glu Thr Cys Ser Glu 145 150 155 160

Lys Ser Thr Asn Leu His Asp Tyr Gly Met Leu Leu Pro Cys Gly IIe 165 170 175

Asp Lys Phe Arg Gly Val Glu Phe Val Cys Cys Pro Leu Ala Glu Glu 180 185 190

Ser Asp Asn Val Asp Ser Ala Asp Ala Glu Glu Asp Asp Ser Asp Val 195 200 205

Trp Trp Gly Gly Ala Asp Thr Asp Tyr Ala Asp Gly Ser Glu Asp Lys
210
220

Val Val Glu Val Ala Glu Glu Glu Glu Val Ala Glu Val Glu Glu Glu 225 230 235 240

Glu Ala Asp Asp Glu Asp Glu Asp Glu Asp Glu Val Glu Glu 245 250 255

Glu Ala Glu Glu Pro Tyr Glu Glu Ala Thr Glu Arg Thr Thr Ser Ile 260 265 270

Ala Thr Thr Thr Thr Thr Thr Glu Ser Val Glu Glu Val Val Arg 275 280 285

Glu Val Cys Ser Glu Gln Ala Glu Thr Gly Pro Cys Arg Ala Met Ile 290 295 300

Ser Arg Trp Tyr Phe Asp Val Thr Glu Gly Lys Cys Ala Pro Phe Phe 305 310 315 320

Tyr Gly Gly Cys Gly Gly Asn Arg Asn Asn Phe Asp Thr Glu Glu Tyr 325 330 335

Cys Met Ala Val Cys Gly Ser Ala Met Ser Gln Ser Leu Leu Lys Thr 340 345 350

Thr Gln Glu Pro Leu Gly Arg Asp Pro Val Lys Leu Pro Thr Thr Ala 355 360 365 Ala Ser Thr Pro Asp Ala Val Asp Lys Tyr Leu Glu Thr Pro Gly Asp 370 375 380

Glu Asn Glu His Ala His Phe Gln Lys Ala Lys Glu Arg Leu Glu Ala 385 390 395 400

Lys His Arg Glu Arg Met Ser Gln Val Met Arg Glu Trp Glu Glu Ala 405 410 415

Glu Arg Gln Ala Lys Asn Leu Pro Lys Ala Asp Lys Lys Ala Val Ile 420 425 430

Gln His Phe Gln Glu Lys Val Glu Ser Leu Glu Gln Glu Ala Ala Asn 435 440 445

Glu Arg Gln Gln Leu Val Glu Thr His Met Ala Arg Val Glu Ala Met 450 455 460

Leu Asn Asp Arg Arg Leu Ala Leu Glu Asn Tyr Ile Thr Ala Leu 465 470 475 480

Gln Ala Val Pro Pro Arg Pro Arg His Val Phe Asn Met Leu Lys Lys 485 490 495

Tyr Val Arg Ala Glu Gln Lys Asp Arg Gln His Thr Leu Lys His Phe 500 505 510

Glu His Val Arg Met Val Asp Pro Lys Lys Ala Ala Gln Ile Arg Ser 515 520 525

- Gln Val Met Thr His Leu Arg Val IIe Tyr Glu Arg Met Asn Gln Ser 530 535 540
- Leu Ser Leu Leu Tyr Asn Val Pro Ala Val Ala Glu Glu Ile Gln Asp 545 550 555 560
- Glu Val Asp Glu Leu Leu Gln Lys Glu Gln Asn Tyr Ser Asp Val 565 570 575
- Leu Ala Asn Met IIe Ser Glu Pro Arg IIe Ser Tyr Gly Asn Asp Ala 580 585 590
- Leu Met Pro Ser Leu Thr Glu Thr Lys Thr Thr Val Glu Leu Leu Pro 595 . 600 605
- Val Asn Gly Glu Phe Ser Leu Asp Asp Leu Gln Pro Trp His Ser Phe 610 620
- Gly Ala Asp Ser Val Pro Ala Asn Thr Glu Asn Glu Val Glu Pro Val 625 630 635 640
- Asp Ala Arg Pro Ala Ala Asp Arg Gly Leu Thr Thr Arg Pro Gly Ser 645 650 655
- Gly Leu Thr Asn lle Lys Thr Glu Glu lle Ser Glu Val Lys Met Asp 660 665 670

Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu 675 680 685

Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala IIe IIe Gly 690 695 700

Leu Met Val Gly Gly Val Val IIe Ala Thr Val IIe Val IIe Thr Leu 705 710 715 720

Val Met Leu Lys Lys Gln Tyr Thr Ser IIe His His Gly Val Val 725 730 735

Glu Val Asp Ala Ala Val Thr Pro Glu Glu Arg His Leu Ser Lys Met 740 745 750

Gin Gin Asn Gly Tyr Glu Asn Pro Thr Tyr Lys Phe Phe Glu Gin Met 755 760 765

GIn Asn 770

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Val Met Leu Lys Lys Lys 1 5